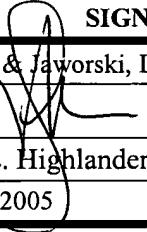
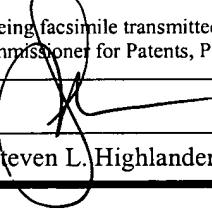


JPL/632

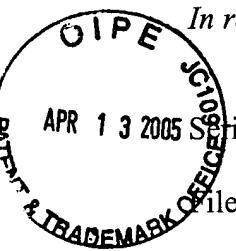
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| TRANSMITTAL FORM | | Application Number: 10/003,669 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Filing Date: November 1, 2001 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | First Named Inventor: Robert H. Broyles | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Art Unit: 1632 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Examiner Name: Janice Li Qian | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Total Number of Pages in this Submission : _____ | | Attorney Docket Number: OMRF:027US | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ENCLOSURES (check all that apply) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <table border="0"> <tr> <td><input type="checkbox"/> Fee Transmittal Form</td> <td><input type="checkbox"/> Drawings(s) _____</td> <td><input type="checkbox"/> After Allowance Communication to TC</td> </tr> <tr> <td><input type="checkbox"/> Fee Attached</td> <td><input type="checkbox"/> Licensing-related Papers</td> <td><input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences</td> </tr> <tr> <td><input type="checkbox"/> Amendment/Reply</td> <td><input type="checkbox"/> Petition</td> <td><input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)</td> </tr> <tr> <td><input type="checkbox"/> After Final</td> <td><input type="checkbox"/> Petition to Convert to a Provisional Application</td> <td><input type="checkbox"/> Proprietary Information</td> </tr> <tr> <td><input type="checkbox"/> Affidavits/declaration(s)</td> <td><input type="checkbox"/> Power of Attorney, Revocation, Change of Correspondence Address</td> <td><input type="checkbox"/> Status Letter</td> </tr> <tr> <td><input type="checkbox"/> Extension of Time Request</td> <td><input type="checkbox"/> Statement under 37 CFR §3.73(b)</td> <td><input checked="" type="checkbox"/> Other Enclosure(s) (please identify below)</td> </tr> <tr> <td><input type="checkbox"/> Express Abandonment Request</td> <td><input type="checkbox"/> Designation of Patent Practitioners</td> <td><input type="checkbox"/> Check in the amount of</td> </tr> <tr> <td><input type="checkbox"/> Information Disclosure Statement</td> <td><input type="checkbox"/> Terminal Disclaimer</td> <td><input type="checkbox"/> Authorized to be charged to deposit account if check insufficient or inadvertently omitted Deposit account number: <u>50-1212</u></td> </tr> <tr> <td><input type="checkbox"/> Form PTO-1449</td> <td><input type="checkbox"/> Request for Refund</td> <td><input type="checkbox"/> Sequence Statement</td> </tr> <tr> <td><input type="checkbox"/> References _____</td> <td><input type="checkbox"/> CD, Number CD(s) _____</td> <td><input type="checkbox"/> Paper Copy of Sequence Listing</td> </tr> <tr> <td><input type="checkbox"/> Certified Copy of Priority Documents</td> <td><input type="checkbox"/> Landscape Table on CD</td> <td><input type="checkbox"/> Computer Readable Form (CRF)</td> </tr> <tr> <td><input type="checkbox"/> Reply to Missing Parts/ Incomplete Application</td> <td></td> <td><input checked="" type="checkbox"/> Postcard</td> </tr> <tr> <td><input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53</td> <td></td> <td><input checked="" type="checkbox"/> Declaration of Dr. Robert H. Broyles</td> </tr> <tr> <td><input type="checkbox"/> Declaration(s) _____</td> <td></td> <td><u>Under 37 C.F.R. § 1.132</u></td> </tr> <tr> <td><input type="checkbox"/> Copy of Notice of Missing Parts</td> <td></td> <td></td> </tr> </table> | | | <input type="checkbox"/> Fee Transmittal Form | <input type="checkbox"/> Drawings(s) _____ | <input type="checkbox"/> After Allowance Communication to TC | <input type="checkbox"/> Fee Attached | <input type="checkbox"/> Licensing-related Papers | <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences | <input type="checkbox"/> Amendment/Reply | <input type="checkbox"/> Petition | <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) | <input type="checkbox"/> After Final | <input type="checkbox"/> Petition to Convert to a Provisional Application | <input type="checkbox"/> Proprietary Information | <input type="checkbox"/> Affidavits/declaration(s) | <input type="checkbox"/> Power of Attorney, Revocation, Change of Correspondence Address | <input type="checkbox"/> Status Letter | <input type="checkbox"/> Extension of Time Request | <input type="checkbox"/> Statement under 37 CFR §3.73(b) | <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below) | <input type="checkbox"/> Express Abandonment Request | <input type="checkbox"/> Designation of Patent Practitioners | <input type="checkbox"/> Check in the amount of | <input type="checkbox"/> Information Disclosure Statement | <input type="checkbox"/> Terminal Disclaimer | <input type="checkbox"/> Authorized to be charged to deposit account if check insufficient or inadvertently omitted Deposit account number: <u>50-1212</u> | <input type="checkbox"/> Form PTO-1449 | <input type="checkbox"/> Request for Refund | <input type="checkbox"/> Sequence Statement | <input type="checkbox"/> References _____ | <input type="checkbox"/> CD, Number CD(s) _____ | <input type="checkbox"/> Paper Copy of Sequence Listing | <input type="checkbox"/> Certified Copy of Priority Documents | <input type="checkbox"/> Landscape Table on CD | <input type="checkbox"/> Computer Readable Form (CRF) | <input type="checkbox"/> Reply to Missing Parts/ Incomplete Application | | <input checked="" type="checkbox"/> Postcard | <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53 | | <input checked="" type="checkbox"/> Declaration of Dr. Robert H. Broyles | <input type="checkbox"/> Declaration(s) _____ | | <u>Under 37 C.F.R. § 1.132</u> | <input type="checkbox"/> Copy of Notice of Missing Parts | | |
| <input type="checkbox"/> Fee Transmittal Form | <input type="checkbox"/> Drawings(s) _____ | <input type="checkbox"/> After Allowance Communication to TC | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> Fee Attached | <input type="checkbox"/> Licensing-related Papers | <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> Amendment/Reply | <input type="checkbox"/> Petition | <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> After Final | <input type="checkbox"/> Petition to Convert to a Provisional Application | <input type="checkbox"/> Proprietary Information | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> Affidavits/declaration(s) | <input type="checkbox"/> Power of Attorney, Revocation, Change of Correspondence Address | <input type="checkbox"/> Status Letter | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> Extension of Time Request | <input type="checkbox"/> Statement under 37 CFR §3.73(b) | <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> Express Abandonment Request | <input type="checkbox"/> Designation of Patent Practitioners | <input type="checkbox"/> Check in the amount of | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> Information Disclosure Statement | <input type="checkbox"/> Terminal Disclaimer | <input type="checkbox"/> Authorized to be charged to deposit account if check insufficient or inadvertently omitted Deposit account number: <u>50-1212</u> | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> Form PTO-1449 | <input type="checkbox"/> Request for Refund | <input type="checkbox"/> Sequence Statement | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> References _____ | <input type="checkbox"/> CD, Number CD(s) _____ | <input type="checkbox"/> Paper Copy of Sequence Listing | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53 | | <input checked="" type="checkbox"/> Declaration of Dr. Robert H. Broyles | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> Declaration(s) _____ | | <u>Under 37 C.F.R. § 1.132</u> | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> Copy of Notice of Missing Parts | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <p>Remarks: Should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski L.L.P. Account No.: 50-1212/OMRF:027US/SLH.</p> | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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|---|---|----------|-----------------------|
| SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT | | | |
| Firm Name | Fulbright & Jaworski, L.L.P. | | Customer Number 32425 |
| Signature |  | | |
| Printed Name | Steven L. Highlander | Reg. No. | 37,642 |
| Date | April 11, 2005 | | |

| | | | |
|---|----------------------|---|----------------|
| CERTIFICATE OF TRANSMISSION/MAILING | | | |
| I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below: | | | |
| Signature | |  | |
| Typed or Printed Name | Steven L. Highlander | Date | April 11, 2005 |

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



In re Application of:
Broyles *et al.*

Serial No.: 10/003,669

Filed: November 1, 2001

For: GENE REGULATION THERAPY
INVOLVING FERRITIN

Group Art Unit: 1632
Examiner: Janice Li Qian
Atty. Dkt. No.: OMRF:027US/SLH

| | |
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| CERTIFICATE OF MAILING 37 C.F.R. § 1.8 | |
| I hereby certify that this correspondence is being deposited with the U.S. Postal Service as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date below: | |
| April 11, 2005 _____ Date | _____ Steven L. Highlander <i>[Handwritten signature over the date and name]</i> |

DECLARATION OF DR. ROBERT H. BROYLES UNDER 37 C.F.R. §1.132

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

I, the undersigned, do declare that:

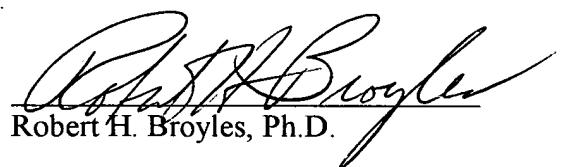
1. I am a citizen of the United States. I am a named inventor on the above-captioned application. I currently hold the position of Professor in the Department of Biochemistry & Molecular Biology at Oklahoma University Health Science Center, and Research Member, in the Free Radical Biology & Aging Research Program at the Oklahoma Medical Research Foundation. A copy of my *curriculum vitae* is attached.

2. In FIG. A (attached), we present a Western blot and an associated bar graph that show induction of the endogenous FtH gene in human cells (NT-2 cells) by abscissic acid added to the medium for 8 days. We have also found this induction of FtH by the same compound in human K562 cells (not shown).
3. In FIG. B (attached), we show initial data from a transgenic mouse made to express human FtH in definitive erythroid cells that are elaborated by the fetal liver beginning in mid-gestation. These red blood cells are the first to express the adult beta-globin genes of the mouse, and the construct in which we inserted the FtH gene was made to direct expression of FtH only in these cells and at the same time as the adult mouse beta-globin. The strain of mouse from which these initial data were collected has *two* types of adult beta-globin genes, beta-major (which accounts for 60% of the expression) and beta-minor (40%). The *key* to this experiment is that *only* the beta-major globin gene of the mouse has the CAGTGC DNA motif that is the core of the FtH binding site; the beta-minor globin gene lacks this site. Thus, when the human FtH transgene is activated in the definitive mouse red cells, the expression of the mouse beta-major globin gene will be repressed but the beta-minor gene will *not* be repressed because it lacks the FtH repression site. So, the transgenic mice mice will be expected to be born alive but have a reduced beta-major/beta-minor ratio and a mild beta-thalessemia due to excess alpha-globin chains (because the mouse has no fetal globin gene to up-regulate in place of beta-major). The presence of "target cells" (red blood cells with a dark spot in the center) in the blood smear of these transgenics and the reduced beta-major/beta-minor ratio seen on

the UT-PAGE globin gel constitute evidence that human FtH can function as a beta-globin gene repressor in a living animal.

4. I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

March 8, 2005
Date


Robert H. Broyles, Ph.D.

CURRICULUM VITAE

Robert H. Broyles, Ph.D.

**Professor of Biochemistry & Molecular Biology
The University of Oklahoma Health Sciences Center
Oklahoma City, Oklahoma**



Personal Data

Date of birth: 2/16/43

S.S. Number: 233-68-6864

Place of birth: Kingsport, Tennessee
Broyles

Family: Wife: Dianne Fields

Addresses: Dept. of Biochemistry &
Molecular Biology
Univ. of Oklahoma Health Sciences Center

Telephones: (405)271-2227, ext. 1213
or ext. 1215
FAX: 405/271-3092

212 NW 20th Street
Oklahoma City, OK 73103

(405)525-5802

Educational Background

B.S., 1965

(in chemistry; minor in physics and mathematics) (advisor, Dr. P.J. Hamrick)

Wake Forest College
Winston-Salem, North Carolina

Embryology Course, summer, 1969

(with Dr. Malcolm Steinberg)

Marine Biological Laboratory
Woods Hole, Massachusetts

Ph.D., 1970

(with Dr. C. F. Strittmatter)

(in biochemistry; minor in microbiology and physiology)

Title of dissertation: Development and Characteristics of Glucose-6-phosphate
and 6-Phosphogluconate Dehydrogenases in the Sea Urchin and the Frog.

Dept. of Biochemistry, The Bowman Gray School of Medicine
of Wake Forest University, Winston-Salem, North Carolina

Postdoctoral, 1970-72

(with Dr. Earl Frieden)

(biochemistry of amphibian metamorphosis)

Dept. of Chemistry, Florida State University
Tallahassee, Florida

Professional Experience

| | |
|---|--------------|
| Research Assistant (with Dr. R.W. Cowgill) Dept. of Biochemistry Bowman Gray School of Medicine Winston-Salem, North Carolina | summer, 1966 |
| Research Associate, Dept. of Chemistry Florida State University Tallahassee, Florida | 1970-1972 |
| Assistant Professor, Department of Zoology, Univ. of Wisconsin-Milwaukee | 1972-1977 |
| Member of the Graduate Faculty, Univ. of Wisconsin-Milwaukee | 1972-1977 |
| Member, Center for Great Lakes Studies, Univ. of Wisconsin | 1975-1977 |
| Tenure approved, UW-Milwaukee | 1977 |
| Associate Professor, Department of Biochemistry and Molecular Biology, College of Medicine Univ. of Oklahoma Health Sciences Center | 1977-1985 |
| Associate Professor of Dental Biochemistry College of Dentistry Univ. of Oklahoma Health Sciences Center | 1977- |
| Member of the Graduate Faculty, University of Oklahoma | 1977-present |
| Tenured, University of Oklahoma | 1979 |
| Professor of Biochemistry and Molecular Biology University of Oklahoma Health Sciences Center | 1985- |
| Adjunct Professor, Department of Pediatrics University of Oklahoma College of Medicine | 1988- |

| | |
|---|---------------------|
| Senior Scientist, National Institutes of Health, NIDDK, Division of Kidney, Urologic and Hematologic Diseases | 1989, 1990 |
| Guest Worker, National Institutes of Health, NIDDK, Laboratory of Chemical Biology | 1989-94; 1995-97 |
| Assistant Director, M.D./Ph.D. Program, College of Medicine, University of Oklahoma | 1991-99 |
| Visiting Scientist, Free Radical Biology & Aging Research, Oklahoma Medical Research Foundation | 1999-2001 |

Research Member, Free Radical Biology & Aging Research, 2001-
Oklahoma Medical Research Foundation

Other Experience

Invited Participant, 6th Workshop on Molecular Techniques for
Developmental Biologists, sponsored by the National Science
Foundation, at the University of California, San Diego, July
2-28, 1973.

Lecturer, Embryology Course, Marine Biological Laboratory, Woods
Hole, Massachusetts, August, 1983.

Sabbatical, Marine Biological Laboratory, Woods Hole,
Massachusetts, 6/83 - 11/83.

Invited Participant, Gordon Conference on Red Cells, Plymouth State
College, Plymouth, New Hampshire, 1985, 1987, 1989.

Invited Speaker, International Conference on *New Trends in the Treatment of
Hemoglobinopathies and Thalassemias*, Paris, France, September 8-12, 1994.

Invited Session Chair, 10th NIH Conference on Hemoglobin Switching, 1996

Invited Participant, NIH Hemoglobin Switching Conferences, Airlie House, Virginia, &
University of Washington, Seattle/Rosario Resort, Orcas Island, WA, 1978,
1980, 1982, 1984, 1986, 1988, 1990, 1992, 1994, 1996, 2000, **2004**.

Invited Participant/Presenter, 13th NIH Conference on Hemoglobin Switching, St. John's

College, Oxford, England, September 11, 2002.

Professional Societies

American Association for the Advancement of Science, 1965-present
American Association of Laboratory Animal Science, 1987
American Association for Cancer Research, 2003-
American Chemical Society, 1966-1972
American Society of Biological Chemists/Amer.Soc.Biochem. & Molecular Biol., 1985-2005
American Society for Cell Biology, 1977-1999
American Society of Gene Therapy, 1998-2005
American Society of Hematology, 1986-present
American Society for Microbiology, 1986-1988
American Society of Zoologists, 1971-1994
International BioIron Society (IBIS), 2003-
International Society of Differentiation, 2000-
New York Academy of Sciences, 1978-1980: 1990-1992
Oklahoma Academy of Sciences, 1981-1982
Oxygen Society, 2000-2001 [became SFBM, below]
Society for Developmental Biologists, 1973-present
Society for Experimental Biology and Medicine, 1978-1980
Society for Free Radical Biology & Medicine, 2001-
Society of Sigma Xi, 1973-present; chapter Pres.-elect, 1988-89, 1990-91; Chapter President,
1991-92; Past Pres., 1992-93.

Awards and Honors

(See list of Patents and Research Grants Received, below.)

| | |
|---|-----------|
| Honorary Scholarship, Wake Forest College | 1961-1963 |
| Honorary Fraternities (undergraduate), chemistry and mathematics | 1963-1965 |
| NDEA Title IV Predoctoral Fellowship | 1965-1968 |
| Wilder Fellowship, Bowman Gray School of Medicine | 1968-1970 |
| NIH Postdoctoral Fellowship (Individual NRSA) | 1970-1972 |
| Elected to Sigma Xi (Marquette Chapter) | 1973 |
| Nominee, Aesculapian Award (for teaching), College of Medicine, Univ. of Oklahoma Health Sciences Center | 1979 |
| Distinguished Service Award, Dept. of Bioc. & Mol. Biol., Univ. of Oklahoma Health Sciences Center | 1982 |
| Elected to membership, American Society of Biological Chemists | 1985 |
| Elected to membership, American Society of Hematology | 1986 |
| MASUA (Mid-America State Universities Association) Honor Lecturer | 1988-89 |

(continued)

Awards and Honors (continued)

| | |
|---|------|
| Elected to membership, American Association for Cancer Research | 2003 |
| Elected to membership, International BioIron Society | 2003 |

Honorary Biographical Listings:

American Men & Women of Science, 19th Edition
Who's Who in the South and Southwest, 24th Edition
Who's Who in American Education, 5th Edition
Who's Who in the World, 13th Edition
Who's Who in Science and Engineering, 2nd Edition
Intrnlt. Directory of Distinguished Leadership, 6th Ed.(nominated)
Men of Achievement, 17th Edition (nominated)

Member, NIH Council/Study Sections/Site Visit Teams:

| | |
|---|-------------|
| NCI, Study Section Member, RFA for Marine/Freshwater Models for Carcinogenesis | 1986 |
| NIDDK, DKUHD, SBIR Grants, Internal Review Committee | 1989 |
| NIDDK, DKUHD, Conference Grants Review Committee | 1989, 1990 |
| NIDDK, National Advisory Council, Program Representative, DKUHD | 1989, 1990 |
| NHLBI, Sickle Cell Center Site Visit Team | March, 1992 |
| NHLBI, Sickle Cell Center Site Visit Team | April, 1992 |
| NHLBI, Sickle Cell Center Site Visit Team | May, 1992 |
| NHLBI, Study Section Member, RFA on Gene Therapy for Sickle Cell Disease | June, 1994 |
| NHLBI, Study Section (Ad hoc), Training Grant Review | Oct., 1994 |
| NHLBI, Study Section (Ad hoc), Training Grant Rev. | May, 1995 |
| NHLBI, Study Section Member, Gene Therapy for Sickle Cell Disease, Program Projects | June, 1995 |
| NHLBI, Study Section Member, RFA on Sickle Cell Disease Treatments, | June, 1996 |
| NHLBI, Special Emphasis Panel, Comprehensive Sickle Cell Centers | May, 1997 |

Current Research Interests

Regulation of gene expression during development
(particularly, developmental hemoglobin switching)
Sickle Cell Disease: molecular approaches to treatments
Role of iron-binding proteins in gene regulation
Carcinogenesis in vitro (especially, hepatocarcinogenesis
studied with liver organ cultures)
Use of the natural iron chelator, Ferritin-H, in treating neurodegenerative diseases
“Back-Burner” Research Interests (can be reactivated):
Model systems in developing amphibians (embryos, larvae, organ explant cultures)
Effects of environmental pollutants (e.g., PCBs, polychlorinated
biphenyls) on development and birth defects

Current Teaching Interests

Molecular biology (e.g., regulation of gene expression)
Molecular basis, diagnosis & proposed treatment of genetic diseases
Molecular & cellular basis of new biotechnologies
Cellular differentiation and carcinogenesis
Developmental biology and birth defects
General biochemistry, general biology, cell biology
History of Scientific Thought in Biochemistry and Molecular Biology

Current Interests in Administration

To stimulate and encourage research collaborations among scientists
and physicians with related interests
To help encourage the use of a variety of extramural funding
mechanisms for research
To encourage and promote interdisciplinary approaches to education and research

Patents Pending

1. **Broyles, R.H.**, and Floyd, R.A. "Gene Regulation Therapy Involving Ferritin" U.S. Patent Applic. Ser. No. 60/245,003 (Pending).
2. **Broyles, R.H.**, and Floyd, R.A., "Gene Regulation Therapy Involving Ferritin." European PA No. 01992721.9 (Pending).
3. **Broyles, R.H.**, Roth, A.C., Floyd, R.A., and Belegu, V. "Abscissic Acid and Derivatives Thereof for the Treatment of Diseases." U.S. Provisional Patent Application OMRF:067USP1) written for submission.

Research Grants Awarded (Principal Investigator on all)

| | <u>dates</u> | <u>agencies</u> | <u>titles</u> |
|----|--------------|--|---|
| 1. | 1970-1972 | NIH, NHLBI (Indiv. NRSA) | Regulation of globin mRNA synthesis during metamorphosis |
| 2. | 1973-1977 | Research Corporation (Cottrell Grant) | Effect of thyroid hormones on the metamorphic hemoglobin transition. |
| 3. | 1974-1975 | Grad.Coll., UW-Milw. | Effects of the larval lampicide TFM on red blood cell differentiation in the sea lamprey <u>Petromyzon marinus</u> . |
| 4. | 1975 | Center for Great Lakes | Effects of the lampicide TFM (3-trifluoro-methyl-4-nitrophenol) UW-Mil. Studies, on hemoglobin synthesis by the sea lamprey and other species. |
| 5. | 1975-1976 | NOAA (U.S. Sea Grant Program) | Effects of polychlorinated biphenyls on the early development of white fish. |
| 6. | 1975-1976 | Grad. Coll., UW-Milw. | TFM, an inhibitor of hemoglobin synthesis: How does it work in sea lamprey, and does it do the same thing to Great Lakes fishes? |
| 7. | 1976-1977 | NOAA (U.S. Sea Grant Program) | Effects of PCBs & other chlorinated hydrocarbons on the early development of lake trout and other Great Lake fishes. |
| 8. | 1976-1977 | NIH/NIAMDD (R01) | Differentiation of red blood cells <u>in vitro</u> . |

At OUHSC

| | | | |
|-----|-------------------|---|---|
| 9. | 1977-1979 | NIH/NIAMDD (R01) | Differentiation of red blood cells <u>in vitro</u> . |
| 10. | 1977-1978 | OUHSC Coll. of Med. Small Grant | Regulation of hemoglobin synthesis in red blood cells differentiating <u>in vitro</u> . |
| 11. | 1979-1983 | NIH/NIAMDD (R01) (Competitive continuation of above, retitled/expanded w/ suppl. funds) | Regulation of hemoglobin switching <u>in vivo</u> and <u>in vitro</u> . |
| 12. | 1981 | OUHSC Research Council | An <u>in vitro</u> approach to studying hepatocarcinogenesis. |
| 13. | 1982-1983 | OU Associates Fund | Cloning of a set of developmentally- regulated genes: A tool for deciphering gene control mechanisms. |
| 14. | 1983-1988 | NIH/NIADDKD NIDDK (R01) (2nd competitive continuation) | Regulation of Hb switching <u>in vivo</u> and <u>in vitro</u> . |
| 15. | 1986-1988 | Presbyterian Hlth.Fndtn. PHF | Regulation of Hemoglobin Switching <u>In</u> <u>vivo</u> and <u>In vitro</u> . |
| 16. | 1988-1989 | | Regulation of Hemoglobin Switching <u>In</u> <u>vivo</u> and <u>In vitro</u> . |
| 17. | 1989-1990 | NIH/NIDDK | Contract (IPA), with NIDDK, Div. of Kidney, Urologic & Hematologic Diseases (90% of salary/FB) |
| 18. | 7/91-10/92 | PHF Seed Grant | Silencing Sickle Cell: A Repressor of the Human Beta Globin Gene |
| 19. | 5/92-4/93 | Provost's Postdoct. Fellowship Award | for Dr. Biji T. Kurien, Madras Univ., as matching funds to PHF Seed Grant |
| 20. | 9/96-8/98 | Pres.Hlth.Fndtn. (funded) | "Advances in Human Molecular Genetics" (Distinguished Lecturer Series and Graduate Course) |
| 21. | 9/98-8/2000 | Pres.Hlth.Fndtn. (funded - Compet. Continuation) | "Advances in Human Molecular Genetics" (Distinguished Lecturer Series and Graduate Course) |
| 22. | 02/01/01-01/31/06 | NIH/NCI | R01: "Free Radicals and Choline-deficient Liver Carcinogenesis" 5 R01 CA082506 Co-Investigator (Subcontract) |
| 23. | 02/01/02-01/31/05 | NIH/NCI | R01 Supplement: "Organotypic Liver Cultures and Hepatocarcinogenesis" 3 R01 CA082506-02S1 |
| 24. | 07/01/01–06/30/03 | AHA/OK Affil. | Predoctoral Fellowship for Visar Belegu "Elucidation of the Function and Regulation of |

Ferritin in Atherosclerotic Lesions." PI
Invited Presentations

| <u>Date</u> | <u>Institution/location/society</u> |
|----------------|--|
| 1. Mar.,1972 | Zoology, Univ.of Wisconsin-Milwaukee |
| 2. Feb.,1973 | Biochemistry, Medical College of Wisconsin |
| 3. Apr.,1974 | 17th International Conference on Great Lakes Research, Hamilton, Ontario |
| 4. June,1975 | Biochemistry, Bowman Gray School of Medicine, Wake Forest Univ., Winston-Salem, NC |
| 5. Nov.,1975 | Biology, Carroll College, Waukesha, WI |
| 6. Nov.,1976 | Biochemistry and Molecular Biology, Univ. of Oklahoma Hlth. Sci. Ctr. |
| 7. Mar.,1977 | 20th International Conference on Great Lakes Research, Ann Arbor, MI |
| 8. Mar.,1978 | ICN-UCLA Symposium, Hemopoietic Cell Differentiation, Keystone, Colorado |
| 9. June,1978 | 1st NIH Conference on Hemoglobin Switching, Battelle Institute, Seattle, WA |
| 10. Apr.,1979 | Biochemistry, Texas Tech Univ. School of Medicine, Lubbock |
| 11. Nov.,1979 | Noble Foundation, Biomedical Branch, Ardmore, Oklahoma |
| 12. Mar.,1980 | Developmental Biology Group, Dept. of Zoology, Univ. of Texas at Austin |
| 13. June,1980 | 2nd NIH Conference on Hemoglobin Switching, Airlie House, Virginia |
| 14. Feb.,1981 | Biology, Pennsylvania State Univ., University Park, PA |
| 15. Mar.,1981 | Oklahoma Medical Research Foundation, Oklahoma City |
| 16. July,1982 | Biochemistry, Bowman Gray School of Medicine, Wake Forest Univ., Winston-Salem, NC |
| 17. Sept.,1982 | 3rd NIH Conference on Hemoglobin Switching, Rosario Resort, Orcas Is., WA |
| 18. Oct.,1982 | Anatomical Sciences, Univ. of Oklahoma Health Sciences Center, Oklahoma City |
| 19. Nov.,1982 | Immunology Discussion Group (Drs. Paul Kincaid and Robert A. Good), Oklahoma Medical Research Foundation (OMRF), Oklahoma City |
| 20. Aug.,1983 | Embryology Course, Marine Biological Laboratory, Woods Hole, Massachusetts |
| 21. Oct.,1983 | Hematology, Dept. of Medicine, Harvard Med.Sch., Brigham & Women's Hospitals, Boston, MA |
| 22. Oct.,1983 | Biology, Mt. Holyoke College, South Hadley, MA |
| 23. Nov.,1983 | Biological Sciences Division, Univ. of Connecticut, Storrs |
| 24. Oct.,1984 | 4th NIH Conference on Hemoglobin Switching, Airlie House, Virginia |
| 25. Aug.,1985 | Gordon Conference on Red Cells, Plymouth State College, Plymouth, NH |
| 26. Nov.,1985 | Anatomical Sciences, Univ. of Oklahoma Health Sciences Center, Oklahoma City |
| 27. Dec.,1985 | Biochemistry & Molecular Biology, OUHSC |
| 28. Dec.,1985 | Hematology Section, Dept. of Medicine, OUHSC |
| 29. Sept.,1986 | Biological Sciences, Texas A & M Univ., College Station |
| 30. Oct.,1986 | 5th NIH Conference on Hemoglobin Switching, Airlie House, Virginia |
| 31. Oct.,1986 | Zoology, Univ. of Oklahoma, Norman |

32. Oct.,1986 Mid-America Molecular Biology Colloquium, OUHSC, Shangri-La Rst., Afton, OK

33. Nov.,1986 Biochemistry & Molecular Biology, OUHSC

34. Aug.,1987 Gordon Conference on Red Cells, Plymouth State College, Plymouth, NH

35. Sept.,1987 Physiology & Biophysics, OUHSC

36. Oct.,1987 2nd Mid-America Molecular Biology Colloquium, OUHSC, Waterford Hotel, Oklahoma City

37. Feb.,1988 Hematology/Oncology, Dept. of Medicine, OUHSC

38. Feb.,1988 Biomedical Research Symposium, Presbyterian Health Foundation, Oklahoma City (platform presentation)

39. Mar.,1988 National Institutes of Health, NIDDK, Div. of Kidney,Urologic & Hematologic Diseases, Bethesda, MD

40. Sept.,1988 6th NIH Conference on Hemoglobin Switching, Airlie House, Virginia

41. 1988-89 MASUA (Mid-America State Universities Association) Honor Lecturer. Presentations on Developmental Regulation of Globin Genes.

42. Nov.,1988 Depts. of Anatomy and Biochemistry, Univ. of Nebraska Med. Ctr., Omaha

43. Apr.,1989 Anatomy and Cell Biology, Univ. of Kansas Med. 4Ctr., Kansas City

44. Apr.,1989 Genetics Section, Dept. of Medicine, Johns Hopkins Univ. School of Medicine, Baltimore

45. May, 1989 Laboratory of Chemical Biology, NIDDK, NIH, Bethesda, MD

46. Aug.,1989 Gordon Conference on Red Cells, Plymouth State College, Plymouth, NH

47. Oct.,1989 Biochemistry, Bowman Gray School of Medicine, Wake Forest Univ., Winston-Salem, NC (In honor of the retirement of Dr. C.F.Strittmatter)

48. June,1990 7th NIH Conference on Hemoglobin Switching, Airlie House, Virginia

49. Mar.,1992 Lady Davis Institute for Medical Research, McGill University, Montreal, Quebec

50. June,1992 8th NIH Conference on Hemoglobin Switching, Rosario Resrt, Orcas Is., WA

51. July,1992 Pediatrics, Univ. of Maryland at Baltimore

52. Nov.,1992 Laboratory of Chemical Biology, NIDDK, National Institutes of Hlth, Bethesda, MD

53. Feb.,1993 Genetics, Endocrinology and Metabolism Sections, Dept. of Pediatrics, OUHSC

54. Mar.,1993 Biology, Univ. of Tulsa, Tulsa, Oklahoma

55. Nov.,1993 Biochemistry & Molecular Biology, OUHSC

56. June,1994 9th NIH Conference on Hemoglobin Switching, Rosario Resrt, Orcas Is.,WA

57. Sept.,1994 INSERM/NIH/WHO/Conference on Sickle Cell Disease & Thalassemias, Paris, France

58. Nov.,1994 Biochemistry, Oklahoma State Univ., Stillwater

59. Jan.,1995 Physiology & Biophysics, OUHSC

60. Sept.,1995 Grand Rounds, Dept. of Pediatrics, OUHSC

61. June,1996 10th NIH Conf. on Hemoglobin Switching, Orcas Is., WA

62. Nov.,1996 Molec.& Cell.Biol.Prgm, Arizona State U., Tempe

63. Dec.,1996 Biochem.& Molec.Biol., Coll. of Med., OUHSC

64. Oct., 1998 11th NIH Conf. on Hemoglobin Switching, Orcas Is., WA
65. Nov., 1998 Free Radical Biol. & Aging Section, Oklahoma Medical Research Foundation
66. June, 2000 12th NIH Conf. on Hemoglobin Switching, Orcas Is., WA
67. Nov., 2000 Oxygen Society, San Diego, CA (platform presentation)
68. Dec., 2000 Free Radical Biology & Aging Section, Okla. Med. Res. Foundation
69. Feb., 2001 **Biochemistry & Molecular Biology, Coll. Of Med., OUHSC**
70. Nov., 2001 **Soc. Free Rad. Biol. & Med., Res.Triangle Park, NC (oral presentation)**
71. Sept.,2002 13th NIH Conf. on Hemoglobin Switching, Oxford, England
72. Sept.,2004 14th NIH Conf. On Hemoglobin Switching, Orcas Island, WA
73. Feb., 2005 Free Radical Biology & Aging Section, Oklahoma Medical Res. Fndtn.

Selected Research Accomplishments (shared with students and collaborators)

First to demonstrate and identify a repressor for the human β-globin gene, the gene mutated in sickle cell disease and to suggest use of gene repression as a phenotypic cure for this genetic disease (with Visar Belegu, Sandeep Shah, Charles Stewart, Quentin Pye, Robert A. Floyd and others)

Proc. Natl. Acad Sci., USA 98, 9145-9150 (2001),

First to demonstrate DNA looping between different parts of a gene promoter using a restriction enzyme and EMSA (electromotive shift assay) (with Biji T. Kurien, Dana Stewart and others)

FASEB J. 8, A1272/#80 (1994).

FASEB J. 9 (6), A1328 (1995).

Sickle Cell Disease & Thalassaemias: New Trends in Therapy 234, 43-51 (1995).

Devel. Biol. 175 (#2), 380 (1996).

Blood 88 (#10), 23b (1996).

Discovered a new, human DNA-binding protein with unique properties which is a candidate repressor of the adult beta globin gene, has properties of a ferritin subunit, and binds an important upstream control region of DNA that contains an iron response element (IRE) consensus sequence (with Dana R. Stewart, Fred Blair, Kim Kyker and others)

Blood 76 (#10, suppl. 1), 56a (1990).

FASEB J. 6 (1), A72, #411 (1992).

FASEB J. 9 (6), A1328 (1995).

Sickle Cell Disease & Thalassaemias: New Trends in Therapy 234, 43-51, (1995).

First to show that trans-acting factors that mediate developmental globin gene switching are conserved between mammals and amphibians, using erythroid heterokaryons formed in vitro (with Janet Barker, David Smith, Larry Ramseyer, Robert Jarman and other students)

Blood 66, 126a (1985); Fed. Proc. 45, 1577 (1986); Blood 68, 138a (1986); J. Cell Biol. 105, 320a (1987); J. Cell Biol. 107, 98a(1989).

Prog. Clin. Biol. Res. 251, 285-294 (1987).

Exptl. Cell Res. 178, 435-448 (1989).

Prog.Clin.Biol.Res. 316 B, 83-96 (1989).

Devel.Biol. 133, 262-271 (1989).

Devel. Genetics 15, 347-355 (1994).

Molecular Biology of Hemoglobin Switching Chap. 26, pp. 313-329 (1995).
Sem. Cell Devel. Biol. 10, 259-265 (1999).

First to clone and sequence a globin cDNA from the bullfrog, Rana catesbeiana. (with David J. Smith, Bruce A. Roe, and Austin F. Riggs)

Blood 68, 138a (1986); J. Cell Biol. 105, 320a (1987); J. Cell Biol. 107, 98a (1989).
J. Biol. Chem. 268, 26961-26971 (1993)..

First to report successful cultures of adult rat liver as a long-term organ culture. (with Martin J. Griffin and Virginia I Stark-Vancs)

Cancer Letters 38, 347-358, 1988.

Delineated the red cell populations and erythropoietic microenvironments involved in developmental hemoglobin switches for the entire life cycle of the bullfrog Rana catesbeiana. (with graduate and medical students)

Nature New Biol. 241, 471-474 (1973).
Science 190, 471-473 (1975).
Devel. Biol. 81, 299-314 (1981).
Proc. Natl. Acad. Sci., USA 79, 5592-5596 (1982).
Devel. Biol. 96, 515-519 (1983).
In Hematopiesis: A Developmental Approach (L.I. Zon, ed.) Oxford Univ. Press (2001).

Discovered that the failure of lake trout to reproduce in Lake Michigan is likely due to PCB contamination, which kills the young at a crucial developmental stage. (with graduate student Martin I. Noveck)

Toxicol. Appl. Pharmacol. 50, 291-298 (1979).
Toxicol. Appl. Pharmacol. 50, 299-308 (1979).

Research Students Mentored

| <u>Ph.D. Students</u> | <u>degree date</u> | <u>Honors, subsequent appts.</u> |
|----------------------------------|--------------------|---|
| 1. Visar Belegu (co-advisor) | 2004 | AHA Predoc Fellowship; Postdoc, John W. McDonald, Johns Hopkins Univ. |
| 2. Christina Bourne (co-advisor) | 2003 | Postdoc, Adam Zlotnick |
| 3. David J. Smith | 1990 | Capt. U.S. Army |
| 4. Phillip B. Maples | 1984 | Postdoc, E.Goldwasser Res. VP, Baxter Hlth.Care |
| 5. Allan R. Dorn | 1982 | Postdoc, Robert Good Fndr/Pres.,SepraTek Res.Sctst, SeraDyne |
| <u>M.D. Students</u> | | |
| 6. Sandeep Shah | 2002 | Presb/Harris Schlr, 1999 |
| 7. Frederick Blair | 1997 | Presb/Harris Schlr, 1992 |
| 8. Anna M. Likos | 1995 | Presb/Harris Schlr, 1992 |
| 9. Donna Sexton Jackson | 1990 | Presb/Harris Schlr, 1988 March of Dimes Schlr,1988 |
| 10. Lorenz T.H. Ramseyer | 1989 | Presb/Harris Schlr,1986,1987 March of Dimes Schlr,1986 |
| 11. Robert N. Jarman | 1989 | Presb/Harris Schlr, 1987 |
| 12. Virginia Stark-Vancs | 1987 | March of Dimes Schlr, 1984 NIH/HHMR Schlr,1985-86 Intern/Res,Georgetown,1987-89 Fellow/Sr. Invest, NCI, 1989-96 Member, Texas Cancer Care, 1996-98 |
| | | Arlington Cancer Ctr./ Director of Clinical Research, Harris Methodist Oncol. |

13. Gary R. Kindell 1984 Intern/Res, UT-SW, Dallas

M.S. Students

| | | |
|------------------------------------|----------------------|-------------------------------|
| 14. Fredrick Blair | 1996 (pend.) | M.D., OUHSC |
| 15. Kimberely D.Kyker | 1995 | |
| 16. Donna Sexton David J. Smith | 1987 1985 | M.D., OUHSC Ph.D., OUHSC |
| Phillip B. Maples | 1981 | Ph.D., OUHSC |
| 17. Allan R. Dorn, | 1979 (Zool.) 1977 | UW- Milwaukee Ph.D., OUHSC |
| 18. Gary R. Kostlan | 1977, UW-Milw. | Dir.,Qual.Cont.,Borden |
| 19. Keith C. Meyer | 1977, UW-Milw. | M.D., UW-Madison |
| 20. Martin I. Noveck | 1977, UW-Milw. | M.D., UW-Madison |
| 21. Martin F. Messar | 1977, UW-Milw. | Chair,Sci.Dept.,Luck,WI |
| 22. William J. Saucier | 1976, UW-Milw. | M.D., UW-Madison |
| 23. Michael J. Deutsch | 1974, UW-Milw. | Astra Pharmaceuticals |

Undergraduates

| | | |
|-----------------------------|------------|---|
| 24. Rebecca Ceraig-Schapiro | 2004-2005 | Honors Thesis, OU; nom. Rhodes Scholar |
| 25. Austin C. Roth | 2003, 2004 | Univ. of Mass., Amherst |
| 26. Katharine M. Harris | 2004 | Univ. of Mass., Amherst |
| 27. Anthony Haney | 1995 | OU Med.Sch., 1996 |
| 28. Dana R. Stewart | 1991-93 | Univ.Central OK |
| 29. Kari A. McBride | 1987-88 | Central State Univ |
| 30. Gerda Breitwieser | 1977 | UW-Milw; Ph.D., Wash.U.; Postdoc, UT-Galveston; Asst/Assoc. Prof., Johns Hopkins Univ. |
| 31. Stuart Berger | 1975 | M.D.,UW; faculty, UW |
| 32. Richard Reid | 1974 | B.A., UW-Milw. |
| 33. Gintaris Dargis | 1974-76 | B.A., UW-Milw. |
| 34. Harry Whelan | 1973-77 | B.A., UW-Milw., M.D., UW; faculty, Vanderbilt |
| <u>High School Students</u> | | |
| 35. Austin Roth | 1999-2000 | Classen Sch. Adv. Studies |
| 36. Mairead Todd | 1998 | Classen Sch. Adv. Studies, Oklahoma City |
| 37. Ashley Sides | 1995 | High Sch., Drumright,OK |
| 38. Jada Benn | 1993-4 | Ntl.Merit Scholar, OU-Norman |
| 39. Thuy H. Do | 1986 | Notre Dame Univ. B.S., Purdue Univ. |

| | | |
|---------------------------------|------------|---------------------|
| 40. Kari A. McBride | 1985-87 | B.S.,Nursing, Emory |
| 41. Sherris A. Harris | 1987, 1988 | N.E. High Sch., OKC |
| 42. Ha Do | 1988 | N.E. High Sch., OKC |
| 43. Melba Moore (Jr. High Sch.) | 1984 | N.E. High Sch., OKC |

Teaching Experience

Approximately 14,000 students taught, 1972-2004.

| <u>Courses taught</u> | <u>Years</u> | <u>University</u> |
|--|-----------------|-------------------|
| *Animal Biology (Zool.101,lect/lab) | 1972-76 | UW-Milwaukee |
| Biology of Man (Biol.102,guest lect.) | 1974-76 | UW-Milwaukee |
| History of Biology (Bot.414, one lect.) | 1973 | UW-Milwaukee |
| Embryology (Zool.360, guest lect.) | 1973 | UW-Milwaukee |
| **Pblms in Developmental Biol.(Biol.420) | 1974-76 | UW-Milwaukee |
| **Cell Biology (Zool.211/lect. & lab.) | 1976 | UW-Milwaukee |
| **Cell Physiology (Zool.470/lect. & lab) | 1973-77 | UW-Milwaukee |
| Undergrad.Seminar in Biol.(Zool. 670) | 1972-73 | UW-Milwaukee |
| **Independ. Study, Undergrad.(Zool. 699) | 1973-77 | UW-Milwaukee |
| **Adv. Independ. Study, Grad.(Zool, 899) | 1973-77 | UW-Milwaukee |
| *Biology Colloquium (Zool. 900) | 1973 | UW-Milwaukee |
| **Adv. Gene Regulation (Zool, 925) | 1973 | UW-Milwaukee |
| **Cell Differentiation (Zool. 925) | 1974 | UW-Milwaukee |
| **Nobel Prizes,Cell/Molec.Biol.(Zool.925) | 1977 | UW-Milwaukee |
| **Molec./Cell.Aspects, Develop.(Zool.926) | 1973 | UW-Milwaukee |
| *Research (Zool. 990) | 1973-77 | UW-Milwaukee |
| Intro.Biochem.(BIOC 4104) | 1977-86 | OUHSC |
| *MSI Biochemistry | 1977-82,1984-98 | OUHSC |
| MS Review Course in Biochemistry | 1978-81 | OUHSC |
| MSI, Medical Molecular Genetics | 1996-2004 | OUHSC |
| *Clinical Correlations(sickle cell disease) | 1991-2004 | OUHSC |
| *Clinical Correlations (carcinogenesis) | 1979 | OUHSC |
| Dental Biochemistry | 1977-82,1984-88 | OUHSC |
| Gen.Biochem.,grad.students(BIOC 5215/8) | 1979-95 | OUHSC |
| Biochem. Lab (BIOC 5224) | 1986-88;1992-96 | OUHSC |
| Molecular Biol.& Genetics(BIOC/MI 5243) | 1991-98 | OUHSC |
| *Grad. Seminar (BIOC 5971/5970) | 1977-99 | OUHSC |
| *Adv. Biochem. Lab (BIOC 6224) | 1979-94;1996 | OUHSC |
| Human Biochemical Genetics(BIOC 6244) | 1979-82 | OUHSC |
| Molecular Oncology(BIOC 6312) | 1977-78 | OUHSC |
| *Cell Biology (BIOC 6223) | 1986-88,1992-99 | OUHSC |
| **Adv.Topics,Human Molec.Genetics(BIOC 6205) | 1993-99 | OUHSC |

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|---|----------------------|--------------|
| Macromolec.Struct.& Fnctn.(BIOC 6215/6214) | 1980-82,92-98 | OUHSC |
| *Molec.Biol.& Biochem. Genetics(BIOC 6235/6234) | 1977-1999 | OUHSC |
| *Research/Doctoral Dissert.(BIOC 6980) | 1977-2004 | OUHSC |
| *Spec.Pblms.Biochem.(BIOC 6990) | 1979,1987-88,1994-98 | OUHSC |
| *Spec.Studies,Med. Students(BIOC/MED 9980) | 1984-88;92 | OUHSC |
| Transcriptional Regulation (BIOC 6340) | 2004-2005 | OUHSC |

*Team-taught courses coordinated one or more times.

**Courses designed, coordinated and taught.

Selected Accomplishments in Teaching and Education

Originator and Coordinator of a graduate course entitled "Advanced Topics in Human Molecular Genetics" (from 1993), which utilizes 12-15 distinguished guest lecturers recognized as leaders in this area

This is an upper-level graduate seminar-discussion course utilizing a combination of local faculty and nationally recognized experts in current molecular approaches to human diseases. A different topic is considered each week, fifteen topics per semester. The format is two class meetings per week, the first being a student discussion of papers from the current literature led by local faculty, and the second consisting of a lecture by an invited expert in the area being considered. After this public lecture, the students spend an hour sequestered with the guest speaker in a relaxed atmosphere discussing items of mutual interest. The guest faculty have included 13 Nobel Laureates and 35 members of the National Academy of Sciences, and all speakers are distinguished in their fields. To our knowledge, this is the best seminar series in molecular biology in the U.S.A. and the best course of its kind in the world.

Research Mentor/Advisor to thirty-nine students at various levels (1975-2001), all of whom have made significant progress and contributions to science at levels beyond their training, including:

Ph.D Student, Alan R. Dorn (Ph.D., 1982), who subsequently did a postdoc with National Academy of Sciences member Robert Good, and was later creator, founder, and president of SepraTek, Inc., the first biotechnology company in Oklahoma City, which successfully marketed a unique one-step clinical procedure for quickly obtaining pure human mononuclear leukocytes from whole blood (under product trade name SepraCell-MN). Dr. Dorn is a Research Director with Seradyne.

M.D. Student, Virginia I. Stark-Vancs (M.D., 1987), who was accepted for the first class of 24 NIH/Howard Hughes Medical Research Scholars (1985-86) and spent a year in the laboratory of gene therapy pioneer Dr. French Anderson (the "father" of gene therapy), as a member of his "gene team." Dr. Stark-Vancs earned the M.D. from OUHSC in 1987, did a residency in internal medicine at Georgetown University, and was a Clinical Research Fellow at the National Cancer Institute, National Institutes of Health, Bethesda, Maryland, from 1991-96. She is currently an oncologist with Texas Cancer Care in Fort Worth.

M.S. Student, Gary R. Kostlan (M.S., 1977), became Director of Quality Control, Cultured Products, for Borden Dairy, Milwaukee, Wisconsin, the nation's largest dairy. He has continued to progress in the dairy industry.

B.S. Student, Gerda Breitwieser (B.S., 1977), went on to a Ph.D. at Washington University in St. Louis, a postdoc at Galveston, and an Assistant Professor, Department of Physiology, Johns Hopkins University School of Medicine, Baltimore. She was recently promoted to Associate Professor with tenure.

High School Student, Thuy H. Do (1986), won third place in biology with his research project in the International Science Fair in Puerto Rico. He subsequently obtained B.S. degree and a commission in the U.S. Navy, from Purdue University.

Originator of Graduate Seminars and Courses in:

Cell Physiology with laboratory (1973)
Molecular & Cellular Aspects of Development (1973)
Cellular Differentiation (1974)
Advances in Gene Regulation (1975)
Cell Biology (1976)
Nobel Prizes in Cellular & Molecular Biology (1977)

Advanced Topics in Human Molecular Genetics (1993 - 1999)

Nominated for an Aesculapian Teaching Award (1979) by the medical student class of 1982.

Taught approximately 14,000 students (1972-2005).

Administrative Experience/University Service

Department of Zoology Committees, UW-Milwaukee:

| | |
|---|-----------------|
| - Course and Curriculum | 1973-75 |
| - Electron Microscope Committee | 1973-77 |
| - Capital Equipment | 1972-73,1975-76 |
| - Ph.D. Program Proposal Committee | 1972-75 |
| - Zoology 101 Course Committee | 1972-76 |
| - Graduate Affairs Committee | 1972-73 |
| - Biology Colloquim | 1973-74 |
| - Faculty Salary Committee | 1976-77 |
| - Public Relations | 1976-77 |
| Instnl.Review Brd.Protectn.Human Subjects, UW-Milw. | 1975-77 |
| Dean's Facul.Advis.Comm.,Coll.of Letters & Sci.,UW-Milw | 1974-77 |
| Graduate Course Comm.,Grad.Coll.,UW-Milw | 1973-75 |
| Search Committee for a Microbiologist, UW-Milw | 1973-75 |
| Microbiology Prgm Planning Comm., UW-Milw | 1974-75 |
| Faculty Senate UW-Milw | 1973-75 |
| # Committee, Jnt Grad. Studies, UW-Milw/Med.Coll.Wis. | 1973-76 |
| # Biol. Sciences Ph.D. Prgm Steering Comm., UW-Milw. | 1975-77 |
| # Joint Course & Curric. Comm.,Zool/Bot, UW-Milw | 1973-74 |
| # Amer. Soc. Zoologists, Campus Rep. UW-Milw | 1975-77 |

Dept. of Biochem.& Molec.Biol.Committees, OUHSC:

| | |
|--|---|
| # - Biochemistry and Molecular Biology Seminar | 1987-88 |
| # - Search Committee for Biochem.Faculty (3) | 1984-85 |
| - Search Committee for Molecular Biologist | 1984-85 |
| # - Search Committee for Molecular Biologist (1) | 1982 |
| - Department Head's Advisory Committee | 1978-79 |
| # - Graduate Admissions and Recruitment | 1977-83,1992 |
| # - Qualifications Comm.for Biochem.Grad.Facul. | 1985-87 |
| - Tenure/Promotions/Joint Appointments Comm. | 1979-80;81-83 |
| # - Comm.to Formulate Guidelines,Tenure/Promotions | 1979-80 |
| # - BIOC 6235 Course Committee | 1981-83,1978-87 |
| # - BIOC 6223 Course Committee | 1991-92 |
| # - BIOC 6502 Course Committee (<u>Chair</u>) | 1991-99 |
| - BioTech MS Degree Task Force | 1995-97 |
| # - General Exam Comm. | 1978-79,1981-82,1986-88,1992-93,1995-2002 |
| - Joint Faculty Review & Evaluation Committee | 1995-2005 |
| # - Fred & Marie Gray Research Award Comm.(Chair) | 1992-2003 |

| | | |
|---|---|--------------------|
| # | - Graduate Student Travel Awards Comm. (<u>Chair</u>) | 1996-2003 |
| | - Graduate Student Awards Committee | 2004-2005 |
| # | - MS I Biochem. Course Committee | 1977-81; 1984-2005 |

College and University-wide Committees

| | | |
|---|--|-----------------|
| # | Res. & Sci. Affairs Comm.,Faculty Senate OUHSC | 1982-84 |
| # | Scientific Merit Subcomm.,Amer.Heart Assoc., OK Affil. Amer. Heart Assoc., OK Affiliate, Res.Policy Comm. | 1978-83 |
| | Search Committee, Dir. of Animal Resources & Facilities | 1980-83 |
| | IACUC (Institutional Animal Care & Use Committee) | 1984-85 |
| | Research Council OUHSC | 1984-88 |
| | Graduate Council OUHSC | 1982 (declined) |
| # | Grad. Coll. Curric.Comm. OUHSC | 1981-84 |
| # | Interdisciplinary Pgm Steering Comm. OUHSC | 1992-94 |
| | Faculty Senate(Alternate), Coll.of Med. OUHSC | 1992-94 |
| | Graduate Education Research Day (GERD): | 1991-94 |
| | - Prize Paper Committee | 1979-80 |
| | - Judge, Basic Sciences | 1992 |
| | Facul.Adviser,Coll.of Med. Grad.Stu.Assoc. OUHSC | 1991-96 |
| | MD/PhD Prgm.Steering Comm.,Coll.of Med. OUHSC | 1991-99 |
| # | Faculty Appeals Board OUHSC/University | 1981-82/1995-99 |

Committees chaired one or more years.

Selected Accomplishments in Administration and Service

Assistant Director, MD/PhD Program, College of Medicine (1991-99)

Encouraged/advised three Native American students to apply for NIH Minority Predoctoral Fellowships from NIGMS and conferred with the NIGMS Program Officer by telephone numerous times. All three applications were funded; one of our students had the highest ranked application in the country. Mentored three students through their first two years of the program. Created a new course in human genetics for MD/PhD and PhD students that brings Nobel Laureates, National Academy members, and other distinguished scientists to campus to meet with these students.

Chair, Search Committee for Faculty in Biochemistry & Molecular Biology (1982, 1984-85)

Wrote advertisements, recruited candidates, and guided the review and ranking of the candidates, which led to short lists of nationally-competitive scientists and the hiring of five outstanding faculty members. Our ad drew over 100 fine applicants.

Member, Search Committee for Director of Animal Resources (1984-85)

The top candidate we recommended was hired - Dr. Gary White, now one of the top animal resources directors in the country.

Chair, Research & Scientific Affairs Committee, Faculty Senate, OUHSC (1982-84)

Recommended to the Provost that the number of research awards for faculty be increased beyond the one available at that time (i.e., the GLC Professorship). This recommendation was transmitted through the Faculty Senate, approved, and instituted as the Provost's Research Awards. This inducement helped double the extramural research funding over a five-year period (1981-1986).

Chair, General Examination Committee, Department of Biochemistry & Molecular Biolgy (1978-79, 1981-82, 1986-88, 1992-97; member, 1997-99; 2000- 2002).

In 1986-88, designed and instituted the format used for 8 years for the General Examination for Admission to Ph.D. Candidacy in Biochemistry and Molecular Biology, which was uniformly endorsed and favored by department faculty. The Exam included two days of written comprehensive tests in biochemistry and molecular biology, a written research proposal in the form of an NIH RO1 grant application, and an oral exam covering both the comprehensive knowledge and research proposal sections. This was among the most rigorous prelim exams in the country and highly valued by students, for three reasons: (1) In studying for the comprehensive portions, the students found that they organized and integrated everything that they had learned. They made a comprehensive set of notes, gained a thorough overview of biochemistry and molecular biology, and saw interrelationships they had not seen before. (2) They learned a very practical skill - how to write a research grant proposal - and had that skill evaluated by successful investigators. (3) Upon successfully completing the exam,

students say that they felt a great sense of accomplishment as well as a marked increase in self-confidence about their ability to teach, to do research, or to do both.

In 1998, a new format was designed that was overwhelmingly accepted by the Graduate Program Faculty. The students now write a research proposal in the NIH format and, after having it evaluated, defend it and answer general knowledge questions related to the proposal in an oral exam.

Chair, Committee to Formulate Guidelines for Faculty Tenure and Promotion in the Department of Biochemistry & Molecular Biology (1979-80)

Formulated the guidelines which were in continuous use for 15 years and were endorsed by five successive department chairmen.

Chair, Committee to Establish Criteria for Graduate Faculty Appointments and Approval to Chair Ph.D. Committees in Biochemistry & Molecular Biology (1985-87)

Formulated the criteria which were in continuous use for 10 years by the department and two of its chairmen.

Chair, Biology Sciences Ph.D. Steering Committee, UW-Milwaukee (1976)

Along with two other Zoology Department faculty and three Botany Department faculty, helped establish the Biological Sciences Ph.D. Program at UW-Milwaukee. Personally designed the poster for advertising the new Ph.D. Program, managed its production, and supervised the mailing of the posters to universities and colleges nationwide, which resulted in a large number of applications to the new program.

Chair, Committee that Formulated and Established Joint Graduate Studies between UW-Milwaukee and the Medical College of Wisconsin (1973-76)

A cooperative program was formulated by faculty from the two institutions and was formally established after being voted upon by each of the separate faculties. The program was a success and is still in existence. It expands and enhances the graduate studies of each institution.

Chair, Joint Course & Curriculum Committee between Zoology and Botany Departments, UW-Milwaukee (1973-74) and chief architect of a new interdisciplinary curriculum

With the collaboration of five other faculty (total of three from Zoology and three from Botany), joint courses were established in three areas of common interest: cell biology, genetics, and basic ecology. This new interdisciplinary curriculum was unanimously approved (with one abstention) by the faculty of both departments, which together numbered 36 members.

Other notable administrative service:

IRB (Institutional Review Board for the Protection of Human Subjects) - 1975-77.

IACUC (Institutional Animal Care and Use Committee) - 1984-88.

Faculty Senate - UW-Milwaukee, 1973-1975;

- Univ. of Oklahoma Health Sci. Ctr.,

1991-94.

NIH, NIDDK - Extramural Program Senior Scientist (administrative consultant) in molecular biology - 1989, 1990. (A more detailed description follows.)

Administrative Experience at the National Institutes of Health
Senior Scientist, National Institutes of Health, 1989 - 1991

A. Position titles: Senior Scientist, Extramural Program

Div. of Kidney, Urologic & Hematologic Diseases (DKUHD) (Dr. Gary E. Striker, Director; Dr. David G. Badman, Asst. Director/Budget, Hematology Program Director) National Institute of Diabetes, and Digestive & and Kidney Diseases (NIDDK)

Senior Scientist (Guest Worker), Intramural Program
Laboratory of Chemical Biology (Dr. Alan N. Schechter, Chief; Dr. Patricia E. Berg, Senior Staff Fellow) NIDDK

B. Tour-of-duty: January 1, 1989 - December 31, 1990

C. Funding: Intergovernmental Personnel Act (IPA), 90% salary/FB

D. Duties: 50% Extramural/50% Intramural:

Extramural: DKUHD, NIDDK (Dr. Gary Striker, Director)

(1) Asst.to Hematology Prgm.Director,Dr. David G. Badman.

(2) Wrote new Initiatives and recent Advances for the Division's Programs, which are part of each year's Implementation Plan that goes to Congress, for FY 1990 and FY 1991.

(3) Organized symposia and workshops in the areas of molecular and cellular biology of kidney and urologic diseases:a) NIDDK 40th Anniversary Symposium:

(a) "*Gene Regulation & Cellular Signaling in the Kidney & Urothelium,*" March 7-9, 1990, at NIH, Bethesda, Maryland.

(b) Hands-on Workshop: "PCR Techniques" (didactic and laboratory), Howard Hughes/Mary Lasker Center, NIH, Oct. 19-21, 1990, Bethesda, Maryland.

(4) Study Sections, Program Representative:

Hematology I & II Study Sections. Molecular Physiology Study Section

(5) NIDDK National Advisory Council Program Representative

(6) Internal Review Panel, Small Business Innovative Research Grants SBIRs)

(7) Internal Review Panel, Conference Grants

(Description of other duties available on request)

Intramural: Lab of Chem.Biol.,NIDDK (Dr. Alan Schechter, Chief)

Community Service (selected items)

Science Education, Elementary and Secondary Schools

Biology demonstrations/presentations

| | |
|--|------------|
| Milwaukee Public Schools, South Milwaukee Elementary, 6th grade | 1974, 1975 |
| Westminster Day School, Oklahoma City, elementary grades | 1980-1984 |
| Montgomery County, MD, public schools, Walter Johnson High School | 1990 |
| Oklahoma School of Science and Math, Oklahoma City (advanced high school) | 1992 |

Mentor, Minority High School Students Summer

| | |
|--|-----------|
| <u>Research Program</u> , University of Oklahoma College of Medicine (six students) | 1986-1996 |
|--|-----------|

Mentor, science fair projects

| | |
|-----------------------------------|------------|
| Junior high school (two students) | 1981, 1984 |
| Elementary school (two students) | 1986, 1988 |

Judge, science fairs

| | |
|---------------------------------------|------|
| Oklahoma City Public Schools | 1985 |
| Westminster Day School, Oklahoma City | 1988 |

Adult Science Education (to the lay public)

| | |
|---|------|
| <u>The Science Bag</u> , Milwaukee, Wisconsin (a public lecture, repeated each Friday for a month) | 1977 |
|---|------|

The Forum, First Unitarian Church, Oklahoma City

(current topics for adults):

| | |
|---|-----------|
| "Use of Animals in Biomedical Research" (with Gary White, D.V.M.) | Dec.,1991 |
| "Diet and Longevity: A Fountain of Youth?" (with B. Connor Johnson, Ph.D.) | Apr.,1992 |
| "Gene Therapy" | Dec.,1992 |
| "The Human Genome Project" | Oct.,1993 |
| "Human Cloning" | Apr.,1994 |

| | |
|---|-------------------------------|
| "DNA Fingerprinting"(w Jay Hanas,speaker) | May, 1995 |
| "How to Make a Unicorn" | May, 1996 |
| "Stem Cells" | Nov., 2000; Nov., 2002 |

Adult Science Education, public (continued)

Lay pulpit, First Unitarian Church, Oklahoma City

Sermon title: "Fried Gene Tomatoes and the King James Bible" (On science and religion; conducted the full service) July,1995

Lay pulpit, First Unitarian Church

Essay title: "For Love of a Frog" (On creativity) June,1996

Lay pulpit, First Unitarian Church

Sermon title: "Hello, Dolly! To Clone or Not To Clone" July, 1998
(Conducted service)

Lay pulpit, Unitarian Universalist Church of Lawton ,OK

Sermon: "Cloning Dolly: Facts, Future, Ethics"

March, 1999

Forum on the Future, Westminster Presbyterian

Church, Oklahoma City (with Dr. Fred Silva, who was the featured speaker); a series of presentations about molecular biology, genes, human health, and ethics:

| | |
|------------|---------------|
| Jan.,1994 | Jan. 28, 1996 |
| Feb.,1994 | Feb. 25, 1996 |
| Mar.,1994 | Mar. 31, 1996 |
| Apr.,1994 | Apr. 28, 1996 |
| June, 1994 | May 19, 1996 |
| | June 30, 1996 |

Science and Religion Dialogue, Westminster Presbyterian

Church; panel member/speaker

Feb. 4, 1997

Science and Religion, II, Westminster Presbyterian

Church; panel member/speaker

Sept., 1998

Adult Leadership in Youth Programs

Unitarian Universalist Association

| | |
|---|------|
| Substitute teacher (elementary grades), Church School, 1st Unitarian Church, Oklahoma City | 1985 |
| YRUU (Young Religious Unitarian Universalists), Career Choices Program, Co-Leader and Mentor, River Road Unitarian Church, Bethesda, MD | 1990 |

Boy Scouts of America (fifteen years of service)

As a youth member and leader (ten years) - ScoWeGo
District, Buckskin Council (Eagle Scout, God and Country Award, Silver Award [Explorer Scouts], Emergency Service Explorer, AOA, Arrow of Light)

| | |
|--|------------|
| <u>As an adult leader (five years) - Dan Beard District,</u> Last Frontier Council, Oklahoma City | 1984, 1985 |
| - Assistant Cub Master, Pack 4, Westminster Presbyterian Church | 1986, 1987 |
| - Cub Master, Pack 4, Westminster Presbyterian Church | 1986 |
| - Asst. Scoutmaster, Troop 240, Central Presbyterian Church | 1987, 1988 |
| - Committee Member, Troop 4, Westminster Presbyterian Church | 1988 |
| - Advancement Chairman, Troop 4 | 1987-1998 |
| - NESA (National Eagle Scout Association) | |

Charitable Contributions (yearly and periodic)

United Way; First Unitarian Church, Oklahoma City; Boy Scouts of America; American Lung Association; Cystic Fibrosis Foundation; March of Dimes; Disabled American Veterans; Salvation Army; Goodwill Industries; Neighbor for Neighbor; REST; Presbyterian Health Foundation.

PUBLICATIONS

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2. Broyles, R. H., and Strittmatter, C. F. Hexose monophosphate shunt dehydrogenases in the developing frog. Compar. Bioc. Physiol. **44B**, 667-676 (1973).
3. Broyles, R. H., and Frieden, E. Sites of haemoglobin synthesis in amphibian tadpoles. Nature **241**, 207-209 (1973).
4. Broyles, R. H., and Deutsch, M. J. Differentiation of red blood cells in vitro. Science **190**, 471-473 (1975).
5. Deutsch, M. J., and Broyles, R. H. Effect of phenylhydrazine on the multiple hemoglobins of Rana catesbeiana tadpoles. Devel. Biol. **46**, 277-231 (1975).
6. Broyles, R. H., and Strittmatter, C. F. Hexose monophosphate shunt dehydrogenases in the sea urchin and the frog: Comparison of some functional properties of the enzymes in vitro. Compar. Bioc. Physiol. **57B**, 249-255 (1977).
7. Broyles, R.H. Hormones. In Laboratory Manual for Animal Biology, D. B. Mooren, ed., Kendall, Hunt Publ. Co., Dubuque, Iowa, pp. 87-89 (all editions, 1974-1977).
8. Broyles, R.H. A Laboratory Guide to Techniques Used in Cell Physiology, Univ. of Wisconsin-Milwaukee, 68 pages, 1974-77.
9. Broyles, R. H., and Noveck, M. I. Uptake and distribution of, 4,5,2',4',5'-hexachlorobiphenyl in fry of lake trout and Chinook salmon and its effects on viability. Toxicol. Appl. Pharmacol. **50**, 299-308 (1979).
10. Broyles, R. H., and Noveck, M. I. Uptake and distribution of 2,5,2',5'-tetrachlorobiphenyl in developing lake trout. Toxicol. Appl. Pharmacol. **50**, 291-298 (1979).
11. Broyles, R. H., Pack, B. M., Berger, S., and Dorn, A. R. Quantification of small amounts of hemoglobin in polyacrylamide gels with benzidine. Anal. Biochem. **94**, 211-219 (1979).

12. Parkinson, A. M., Dorn, A. R., Maples, P.B., and Broyles, R. H. Improved polyacrylamide gel electrophoresis with different amino acids as the trailing constituent. Anal. Biochem. 117, 6-11 (1981).
13. Broyles, R. H., Johnson, G. M., Maples, P. B., and Kindell, G. R. Two erythropoietic microenvironments and two larval red cell lines in bullfrog tadpoles. Devel. Biol. 81, 299-314 (1981).
14. Broyles, R. H. Changes in the blood during amphibian metamorphosis. In Metamorphosis: A Problem in Developmental Biology, 2nd ed. (L. I. Gilbert and E. Frieden, eds.), Chap. 14, Plenum Publ. Co., New York, pp. 461-490 (1981).
15. Broyles, R. H., Dorn, A. R., Maples, P. B., Johnson, G. M., Kindell, G. R., and Parkinson, A. M. Choice of hemoglobin type in erythroid cells of Rana catesbeiana. In Hemoglobins in Development and Differentiation (G. Stamatoyannopoulos & A. W. Nienhuis, eds.), Alan R. Liss, Inc., New York, pp. 179-191 (1981).
16. Dorn, A. R., and Broyles, R. H. Erythrocyte differentiation during the metamorphic hemoglobin switch of Rana catesbeiana. Proc. Natl. Acad. Sci. USA 79, 5592-5596 (1982).
17. Maples, P. B., Dorn, A. R., and Broyles, R. H. Embryonic and larval hemoglobins during the early development of the bullfrog Rana catesbeiana. Devel. Biol. 96, 515-519 (1983).
18. Maples, P. B., Palmer, J. C., and Broyles, R. H. In vivo regulation of hemoglobin phenotypes of developing Rana catesbeiana. Devel. Biol. 117, 337-341 (1986).
19. Broyles, R.H., Palmer, J.C., Ramseyer, L.T.H., Smith, D.J., Jarman, R.N., Do, T.H., and McBride, K.A. Hemoglobin switching across vertebrate classes: Exchange of developmental signals by cell fusion. Prog. Clin. Biol. Res. 251, 285-294 (1987).
20. Maples, P.B., Palmer, J.C., and Broyles, R.H. Determination of hemoglobin expression patterns in erythrocytes of Rana catesbeiana tadpoles. Compar. Biochem. Physiol. 91B, 755-762 (1988).
21. Palakodety, R., Griffin, M.J., and Broyles, R.H. Circulating epoxide hydrolase immunodeterminants in rats bearing hyperplastic nodules induced by 2-acetylaminofluorene. Cancer Letters 38, 347-358 (1988).
22. Barker-Harrel, J., McBride, K.A., and Broyles, R.H. Formation of transient polykaryons by fusion of erythrocytes of different developmental programs. Exptl. Cell Res. 178, 435-448 (1988).

23. Ramseyer, L.T.H., Barker-Harrel, J., Smith, D.J., McBride, K.A., Jarman, R.N., and Broyles, R.H. Intracellular signals for developmental hemoglobin switching. Devel. Biol. 133, 262-271 (1989).
24. Broyles, R.H., Barker-Harrel, J., Ramseyer, L.T.H., McBride, K.A., and Sexton, D.L. Erythroid heterokaryons: a system for investigating the functional role of trans-acting factors in developmental hemoglobin switching. Prog. Clin. Biol. Res. 316B, 83-96 (1989).
25. Kurien, B.T., and Broyles, R.H. Plasmid DNA preparation by heat treatment of Escherichia coli lysates. Anal. Biochem. 213, 174-176 (1993).
26. Smith, D.J., Zhu, H., Kolatkar, P.R., Tam, L.-T., Baldwin, T.O., Riggs, A., Roe, B.A., and Broyles, R.H. The hemoglobins of the bullfrog, Rana catesbeiana. The cDNA-derived amino acid sequences of the alpha chain of adult hemoglobins B and C: Their roles in deoxygenation-induced aggregations. J. Biol. Chem. 268, 26961-26971 (1993).
27. Broyles, R.H., Ramseyer, L.T.H., Do, J.H., McBride, K.A., and Barker, J.C. Hemoglobin switching in Rana/Xenopus erythroid heterokaryons: Factors mediating the metamorphic hemoglobin switch are conserved. Devel. Genetics 15, 347-355 (1994).
28. Broyles, R.H., Blair, F.C., Kyker, K.D., Kurien, B.T., Stewart, D.R., Hala'sz, H., Berg, P.E., and Schechter, A.N. A ferritin-like protein binds to a highly conserved CAGTGC sequence in the β -globin promoter. Sickle Cell Disease and Thalassaemias: New Trends in Therapy (Y. Beuzard, B. Lubin, and J. Rosa, eds.) Colloque INSERM/ John Libbey Eurotext Ltd., vol. 234, pp. 43-51 (1995).
29. Kyker, K.D., Likos, A.M., Blair, F.C., Kurien, B.T., Hala'sz, H., Benn, J., and Broyles, R.H. Hemoglobin switching in heterokaryons: Conservation of trans-acting factors that mediate developmental gene regulation. In Molecular Biology of Hemoglobin Switching (G. Stamatoyannopoulos, ed.) Intercept Ltd., Andover, Hampshire, UK, Chap. 26, pp. 313-329 (1995).
30. Broyles, R.H. (ed.) "Advances in Human Molecular Genetics" A series of 12 videotapes of lectures by distinguished scientists from the 1995 series at the Univ. of Oklahoma Health Sciences Center, Dept. of Biochemistry and Molecular Biology. (Produced by the College of Continuing Education, Univ. of Oklahoma; David Stamps, producer. Copyright 1996, Univ, of Oklahoma.)
31. Kurien, B.T., Scofield, R.H., and Broyles, R.H. Efficient 5' End Labeling of Dephosphorylated DNA. Anal. Biochem. 245, 123-126 (1997).
34. Broyles, R.H. Use of somatic cell fusion to reprogram globin genes. Sem. Cell Devel.

Biol. **10**, 259-265 (1999).

35. Broyles, R.H. "Hemoglobin Switching and Developmental Changes in Erythropoietic Sites and Red Blood Cell Populations of Non-mammalian Vertebrates." In **Hematopoiesis: A Developmental Approach** (L.I. Zon, ed.). Oxford Univ. Press, New York, Chap. 53, pp. 617-637 (2000).
36. Broyles, R.H., Belegu, V., DeWitt, C. R., Shah, S.N., Stewart, C.A., Pye, Q.N., and Floyd, R.A. Specific repression of β -globin promoter activity by nuclear ferritin. *Proc. Natl. Acad. Sci., USA* **98**: 9145-9150 (2001).
37. Guo W-X, Pye QN, Williamson KS, Stewart CA, Hensley KL, Kotake Y, Floyd RA, and **Broyles RH**. Reactive oxygen species in choline deficiency-induced apoptosis in rat hepatocytes. *Free Radic Bio Med* **37**: 1081-1089 (2004).
38. Scofield, RH, Kurien, BT, Ganick, S, McClain, MT, Pye, Q, James, JA, Schneider, RI, **Broyles, RH**, and Hensley, K. Modification of lupus-associated 60 kDa Ro protein with the lipid oxidation product 4-hydroxy-2-nonenal increases antigenicity and facilitates epitope spreading. *Free Radic Bio Med* **38**: 719-728 (2005).
39. Guo W-X, Pye QN, Williamson KS, Stewart CA, Hensley KL, Kotake Y, Floyd RA, and **Broyles RH**. Mitochondrial dysfunction in choline deficiency-induced apoptosis in cultured rat hepatocytes. *Free Radic Bio Med* (submitted, 10/22/04; in revision).
40. **Broyles, RH**, Roth, AC, Todd, M, and Belegu, V. "Nuclear Reprogramming by Cell Fusion." In *Nuclear Reprograming: Methods and Protocols, Methods in Molecular Biology* (S. Pells, ed.), Humana Press, Inc., Totowa, NJ (In press).

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2. **Broyles, R. H.** Hemoglobin synthesis *in vitro* by amphibian kidney and liver. *Fed. Proc.* 31: 844 (1972).
3. Messar, M. F., and **Broyles, R. H.** Effects of TFM exposure on C-14 labeled amino acid incorporation into sea lamprey erythrocyte protein *in vitro* and *in vivo*. (Presented at the 17th Conference on Great Lakes Research, Hamilton, Ontario, May, 1974.) *Oral Presentation*.
4. Deutsch, M. J., and **Broyles, R. H.** Erythropoiesis and hemoglobin synthesis in young bullfrog tadpoles: Multiple hemoglobins, red cell lines and erythropoietic sites. *Fed. Proc.* 33 (#5,pt.II): 1343 (1974). *Oral Presentation*.
5. **Broyles, R. H.**, Berger, S., and Dorn, A. R. Specific hemoglobin synthesis appears to be regulated by erythropoietic microenvironments in bullfrog tadpoles. (Presented at the Midwestern Regional Developmental Biology Conference, Miami Univ., Oxford, Ohio, April 8-10, 1976.)
6. Saucier, W. J., and **Broyles, R. H.** Red blood cell differentiation in bullfrog tadpoles and in juvenile and adult frogs. (Presented at the Midwestern Regional Developmental Biology Conference, Miami Univ., Oxford, Ohio, April 8-10, 1976.)
7. Noveck, M. I., and **Broyles, R. H.** Uptake and distribution of polychlorinated biphenyls (PCBs) by embryos and fry of lake trout and Chinook salmon. (Presented to the 20th Conference on Great Lakes Research, Univ. of Michigan, Ann Arbor, May, 1977.)
8. **Broyles, R. H.**, and Dorn, A. R. Erythropoietic microenvironment-specific hemoglobin synthesis in larval bullfrogs. *J. Supramolec. Struct.*, suppl. 2: 164 (1978). (Presented at the ICN-UCLA Symposium on Hemopoietic Cell Differentiation, Keystone, Colorado, April, 1978.)
9. Dorn, A. R., and **Broyles, R. H.** Density-gradient separation of RBC's of different hemoglobin types. *J. Supramolec. Struct.*, suppl. 2: 164 (1978). (Presented at the ICN-UCLA Symposium on Hemopoietic Cell Differentiation, Keystone, Colorado, April, 1978.)

10. **Broyles, R. H.** Switching of erythropoietic organ-specific larval hemoglobins in organ cultures. (Presented at the 1st Conference on Hemoglobin Switching, co-spon. by NIH and the Univ. of Washington, Seattle, WA, 1978.)
11. **Broyles, R. H.**, and Dorn, A. R. Cross-induction of erythropoietic organ-specific larval bullfrog hemoglobins in organ cultures. *J. Cell Biol.* **79** (#2, pt.2): 26a (1978).
12. Dorn, A. R., and **Broyles, R. H.** Density gradient separation of differentiating red blood cells. *Fed. Proc.* **39**: 1601 (1980).
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14. Dorn, A. R., and **Broyles, R. H.** Hemoglobin switching during development in Rana catesbeiana. *Fed. Proc.* **40** (6): 1629 (1981).
15. **Broyles, R. H.**, Maples, P. B., and Dorn, A. R. Developmental changes in the hemoglobins of the bullfrog Rana catesbeiana. (Presented to the Oklahoma Academy of Science, Enid, OK, Nov. 13, 1981.)
16. Dorn, A. R., and **Broyles, R. H.** Purification and characterization of adult and tadpole erythroid cells during the metamorphic hemoglobin switch of bullfrogs. (Presented to the Oklahoma Academy of Science, Enid, OK, Nov. 1, 1981.)
17. Maples, P. B., and **Broyles, R. H.** Antibodies against individual tadpole and adult bullfrog hemoglobins. (Presented to the Oklahoma Academy of Science, Enid, OK, Nov. 13, 1981.)
18. Smith, D. J., Maples, P. B., Dorn, A. R., Saucier, W. J., Vigoreaux, J., and **Broyles, R. H.** Hemoglobin types, red blood cell classes and erythropoietic loci of the bullfrog, Rana catesbeiana. (Presented at the 41st Annual Symposium of the Society for developmental Biology, **Harvard Univ.**, Cambridge, MA, June 13-17, 1982.)
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20. Dorn, A. R., and **Broyles, R. H.** Developmental changes in purified tadpole and adult erythroid cells during metamorphosis of Rana catesbeiana. (Presented at the 41st Annual Symposium of the Society for Developmental Biology, **Harvard Univ.**, Cambridge, MA, June 13-17, 1982.)

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22. Dorn, A. R., and **Broyles, R. H.** Differentiation of erythrocytes during the metamorphic hemoglobin switch of Rana catesbeiana. (Presented at the 3rd Conference on Hemoglobin Switching, co-sponsored by NIH and the Univ. of Washington-Seattle, Orcas Island, WA, Sept. 12-16,1982.)
23. Maples, P. B., and **Broyles, R. H.** Embryonic and larval erythropoiesis of Rana catesbeiana. (Presented at the First Annual Southwestern Developmental Biology Conference, Univ. of Texas at Arlington, March 24-26, 1983.)
24. **Broyles, R. H.** Developmental Hemoglobin Switching: Changes in globin types, red cell classes, and erythropoietic sites. (**Two invited lectures, presented to the Embryology Course, Marine Biological Laboratory, Woods Hole, Massachusetts**, August 10, 1983.)
25. Maples, P. B., and **Broyles, R. H.** Early erythropoiesis of the bullfrog Rana catesbeiana. *J. Cell Biol.* 97 (#5, pt.2): 56a (1983). (Presented at the 23rd Annual Meeting of the American Society for Cell Biology, San Antonio, Texas, Nov. 29 - Dec. 3, 1983.)
26. Maples, P. B., and **Broyles, R. H.** In vivo regulation of hemoglobin profile of Rana catesbeiana tadpoles. (Presented at the 4th Conference on Hemoglobin Switching, co-sponsored by NIH and the Univ. of Washington-Seattle, Airlie House, Virginia, Sept. 30-Oct. 3, 1984.)
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33. Palmer, J.C., Stark-Vancs, V.I., McBride, K.A., Coalson, R.E., and **Broyles, R.H.** The cell biology of developmental hemoglobin switching in the amphibian Rana catesbeiana. (Poster presented at the Mid-America Molecular Biology Colloquium, Shangri-La Resort, Afton, Oklahoma, Oct. 14-17, 1986.)
34. **Broyles, R.H.**, Palmer, J.C., and Maples, P.B. Developmental regulation of hemoglobin types in Rana catesbeiana: Anemia induces a precocious metamorphic switch in gene expression. (Poster presented at the Mid-America Molecular Biology Colloquium, Shangri-La Resort, Afton, Oklahoma, Oct. 14-17, 1986.)
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48. **Broyles, R.H.** Developmental signaling: Factors that program and trans-regulate globin genes. (Invited oral presentation at the **Oklahoma Biomedical Research Symposium sponsored by the Presbyterian Health Foundation**, the University of Oklahoma Health Sciences Center, and the Oklahoma Medical Research Foundation; held at the Waterford Hotel and the Univ. of Oklahoma Health Sciences Center, Oklahoma City, February 21-23, 1988.)
49. **Broyles, R.H.** Developmental regulation of gene expression: Globin switching as a model. (Oral presentation delivered, by invitation, to extramural and intramural scientists at the **National Institutes of Health, Bethesda, Maryland**, March 16, 1988.)
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54. **Broyles, R.H.** "Developmental Regulation of Globin Genes in Erythroid Heterokaryons." (Seminar presented at The Johns Hopkins University School of Medicine, Hematology "Soup Seminar," Feb. 28, 1989.)
55. **Broyles, R.H.** "Globin Gene Regulation During Development." (A pair of lectures presented at the University of Kansas Medical Center, April 13 & 14, 1989, as a 1988-89 MASUA Honor Lecturer.)
56. Barker-Harrel, J., Ramseyer, L.T.H., Smith, D.J., and **Broyles, R.H.** Cell fusion mediated delivery of trans factors for hemoglobin switching. (Presented at the Gordon Research Conference on Red Cells, Plymouth, NH, Aug. 7-11, 1989.)
57. **Broyles, R.H.** "The Cellular and Molecular Biology of Developmental Hemoglobin Switching." (An invited lecture presented in honor of Dr. C.F. Strittmatter, IV, Odus M. Mull Professor of Biochemistry, on his retirement, October 12, 1989.)
58. Smith, D.J., Baldwin, T.O., Riggs, A.F., Roe, B.A., and **Broyles, R.H.** Sequence of a bullfrog adult alpha globin and its role in deoxygenation-induced hemoglobin aggregation. (7th NIH Conference on Hemoglobin Switching, Airlie House, VA, Sept. 7-11, 1990.)
59. **Broyles, Robert H.** Comparative biology of globin gene expression in vertebrates: Developmental patterns of erythropoietic sites, red cell lines, and hemoglobin types. (Presented at the 7th NIH Conference on Hemoglobin Switching, Airlie House, VA, Sept. 7-11, 1990.)
60. **Broyles, R.H.**, Berg, P.E., and Schechter, A.N. A protein in K562 nuclear extracts with ferritin-like properties binds to 5' regulatory sequences of the human beta globin gene. *Blood* **76** (#10, suppl. 1): 56a (1990). (Presented at the combined meeting of the International

Society of Hematology and the American Society of Hematology, Boston, MA, Nov.28-Dec.4, 1990.)

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Dual roles for ferritin-H: (1) specific repression of the human β -globin promoter mediated by DNA-binding, and (2) regulation of the labile iron pool mediated by metal binding.

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99. **Broyles, R.H.** "Organotypic Liver Cultures for Investigating Hepatocarcinogenesis" Cell Cycle and Tumor Progression Group, OU Cancer Center, Feb. 18, 2003 (Invited presentation).
100. Belegu, V., Stewart, C., Floyd, R.A., **Broyles, R.H.** New Functions of Nuclear Ferritin. OUHSC GREAT Symposium, 2003.
101. **Broyles, R.H.**, Belegu, V., Kurien, B.T., Stewart, C.A., Pye, Q.N., Guo, W-X., Floyd, R.A. Ferritin heavy chain localizes to the nucleus and represses the adult human β -globin gene in cultured cells. **IBIS (International BioIron Society) World Congress on Iron Metabolism**, NIH, Bethesda, MD, May, 4-9, 2003.
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103. **Broyles, R.H.**, Pye, Q.N., Salsman, S.J., Belegu, V., Kotake, Y., Floyd, R.A. Long-lived organotypic rat liver cultures for studying hepatocarcinogenesis. **AACR** (Amer. Assoc. of

- Cancer Research) meeting, Toronto, Canada, Apr. 5-9, 2003. Membership pending. *Cancer Res.* **44**: 554/478 #2440 (2003).
104. **Broyles, R.H. (Session Chair)**, "New (or Recent) Players in the Iron World: Hepcidin and Signaling between Liver, Gut and RE; Nuclear and Mitochondrial Ferritin," at the 13th annual meeting of the *East Coast Iron Club*, University of Pennsylvania Medical Center Campus, Philadelphia, Nov. 14, 2003.
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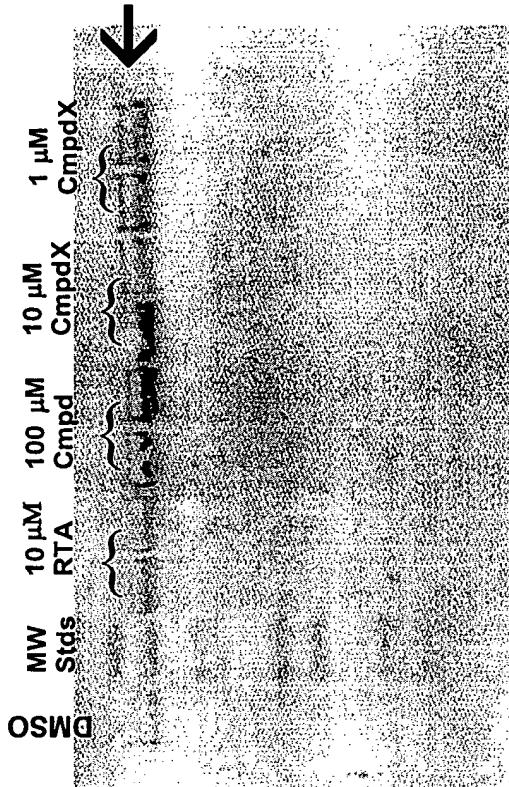
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113. Asada K, Kotake Y, Asada R, Saunders D, **Broyles RH**, Towner RA, Floyd RA. LINE1 hypomethylation in a choline-deficiency induced liver cancer model. (*Presented at the AACR Conference on "Chromatin, Chromosomes, and Cancer Epigenetics," at Waikoloa, Hawaii, Nov. 10-14, 2004.*)
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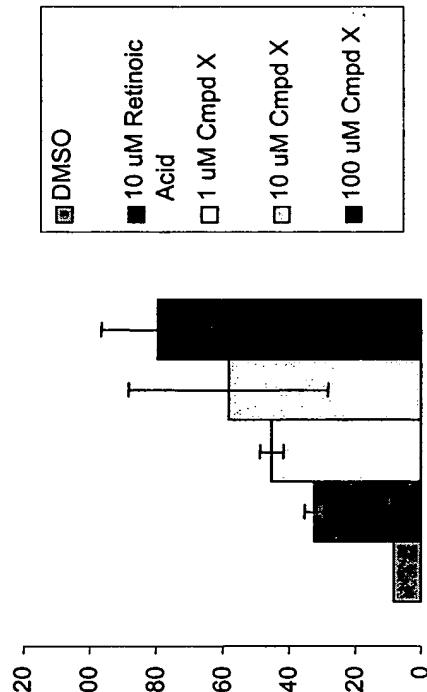
Induction of Fth in Differentiating NT- 2 Human Embryonal Carcinoma Stem Cells



NT 2 (NTERA-2)
cells differentiating into neurons
in spheres as a result of retinoic
acid (RTA) treatment.

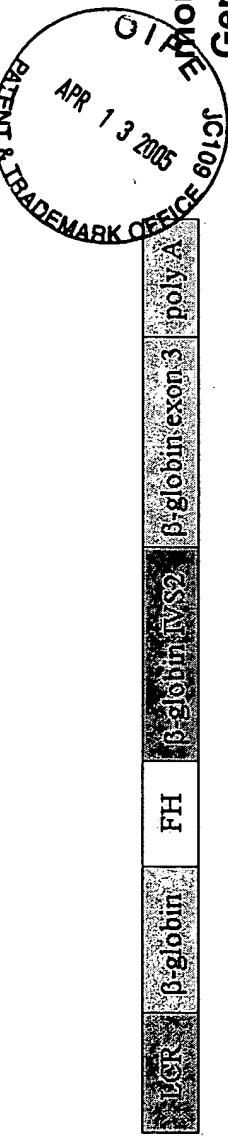


Western blot with antiFth specific serum of lysates of NT 2 cells treated with inducing/differentiating agents in the medium for 8 days. Arrow: Bands of polymerized ferritin heavy chains (Fth).



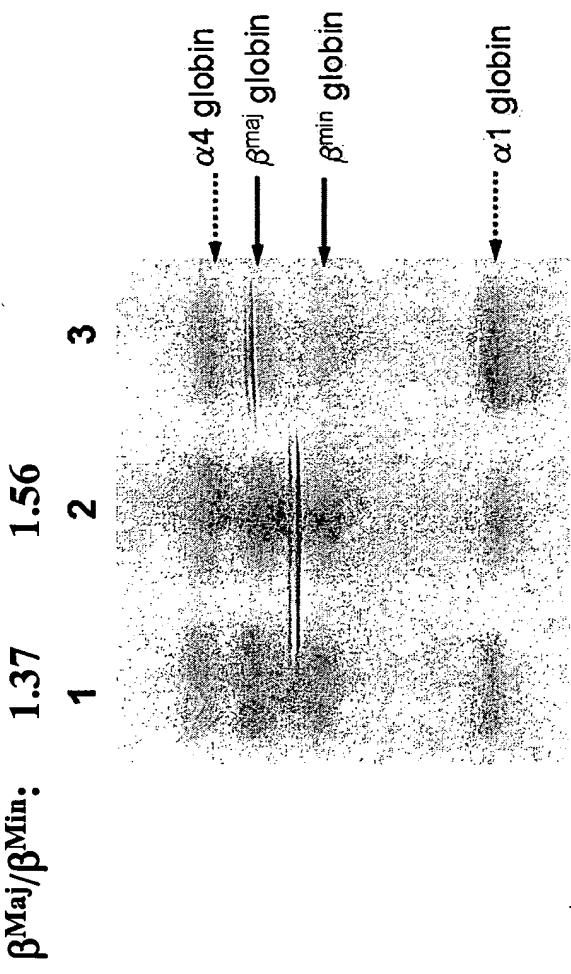
Ferritin H

*FtH Represses β^{Major} -Globin *In vivo* in Transgenic (*FtH*) Mice*



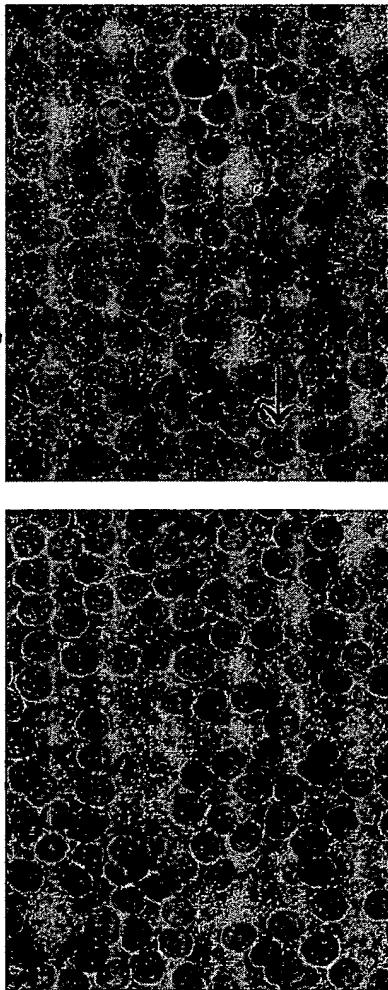
FtH represses the β^{Major} Globin Gene in Transgenic Mice.

(a) Schematic diagram of the human FtH construct used for creation of ferritin transgenics. (b) UT Page electrophoresis of globin chains from an FtH transgenic mouse (lane 1), a non-transgenic mouse (lane 2), and globin standards (lane 3). (c) Blood smears from a non-transgenic mouse (wt) and a transgenic mouse (FtH transgenic). The FtH-Tg mice appear to have a mild β -thalassemia characterized by increased numbers of target cells (arrow) indicative of inclusions due to precipitated excess α -chains.



% Target
Cells:
wt

FtH transgenic 22.6%



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